[biologically active] fragment or variant thereof, wherein the fragment or variant has telomerase catalytic activity [in the cell].

27. (amended) A method of increasing telomerase activity in a cell, comprising expressing in the cell a [TP2 gene] telomerase protein 2 nucleic acid molecule, or a [biologically active] fragment or variant thereof, wherein the fragment or variant has catalytic activity [in the cell].

28. (amended) A method of decreasing telomerase activity in a cell, comprising expressing a [TP2 mutant] telomerase protein 2 variant nucleic acid molecule of SEQ ID NO:13 or SEQ ID NO:19 in a cell, wherein the [mutant] variant does not have [TP2 biological] telomerase protein 2 catalytic activity.

29. (amended) A nucleic acid molecule encoding a [mutant TP2] variant telomerase protein 2 polypeptide, wherein the codon for aspartic acid at amino acid position 868 or 869 of SEQ ID NO:19 is changed to a codon for alanine.

C4 Cont.

30. (amended) A nucleic acid molecule encoding a [mutant TP2] variant telomerase protein 2 polypeptide, wherein the codons for aspartic acid at amino acid positions 868 and 869 of SEQ ID NO:19 are changed to codons for alanine.

Please add the following new claim:

C5 & 6 25

33. (newly added) A transformed or transfected host cell expressing telomerase protein 2 having telomerase catalytic activity.

REMARKS

As a preliminary matter, Applicants acknowledge receipt of a copy of PTO Form-1449, but note that the documents listed on sheet 2 (foreign patent documents) were not initialed by the Examiner. Applicants supplied a copy of each such document with the PTO Form-1449. However, should the Examiner require another copy of each document, Applicants can readily supply them on request. Otherwise, Applicants would appreciate receipt of an initialed copy of sheet 2 of PTO Form-1449.

Several minor amendments have been made to the specification to correct inadvertent word processing errors. On page 32, line 35 of the specification, an article by Merrifield *et al.* is cited listing the year of publication as 1964. In fact, the correct year for that article is 1963. On page 54, line 24, an article

by Strathman *et al.* in the journal *Science* is cited in reference to the plasmid pMOB. The proper publication for this reference is *Proc. Natl. Acad. Sci USA.* A copy of the correct article was supplied by Applicants as item FB in the IDS submitted May 28, 1998. On page 58, line 6, the first author of the cited article in Cancer Research was erroneously listed as "Whitehead". The correct author is Willson. A copy of this article listing Willson as the first author was submitted by Applicants as item FI in the IDS mailed May 28, 1998. On page 67, line 5, "Fields" was listed as the first author of a paper discussing the rat iron regulatory element mRNA. The correct first author is SenGupta. A copy of the cited article, listing SenGupta as the first author was submitted with the IDS filed May 28, 1998 as item ET. Finally, on page 96, lines 25-26, the address of the ATCC has been corrected. The ATCC changed their address after the subject patent application was filed. No new matter is added by these amendments.

Claims 1-32 are pending in the subject patent application and all stand rejected. Claims 22-25 and 31-32 have been withdrawn by the Examiner. As such, claims 1-21 and 26-30 are currently under consideration.

Claims 1, 4, 19, 26, 27, 28, 29, and 30 have been amended herein.

Claim 1 has been amended to recite an isolated nucleic acid molecule, and to substitute "telomerase protein 2" for "TP2". This claim has been further amended to add the computer algorithm and parameters used to calculate percent identity. Support for this amendment can be found in the specification, as for example on page 17, lines 5-13, wherein there is a description of calculating "percent sequence identity". In this description, the FASTA algorithm, the use of default parameters, and the use of the PAM 250 scoring matrix are set forth. Each of these items is now recited in claim 1. Claim 1 has been further amended to recite the parameters that constitute "stringent conditions". Support for this amendment can be found in the specification on page 18, lines 5-14, wherein there is a definition of "stringent conditions" which includes 2 X SSC, 0.1 percent SDS, and temperatures between 55-65C. Each of these parameters is now recited in claim 1.

Claim 4 has been amended herein to recite and isolated nucleic acid molecule and to substitute the word "or" for the word "of". The use of the word "of" was an inadvertent word processing error.

Claim 19 has been amended to recite "telomerase protein 2" instead of "TP2" per the Examiner's suggestion, and to insert the word "molecule" after "nucleic acid".

Claim 26 has been amended to recite "proliferation rate" instead of "proliferation" per the Examiner's suggestion. The phrase "biologically active" has been replaced with the phrase "catalytic activity" to more clearly define the claimed subject matter. Support for the use of "catalytic activity" can be

found throughout the specification as for example, on page 15, line 36 and page 16, line 1, wherein there is a definition of "biologically active" telomerase and fragments which includes "catalytic activity". Claim 26 has been further amended to replace the word "mutant" with the word "variant". Support for this amendment can be found on page 15, line 19 wherein the term "TP2 variant" is described. The amendments serve to more accurately describe the invention as claimed in claim 26.

Claim 27 has been amended to replace the term "TP2" with the term "telomerase protein 2", to replace the phrase "biologically active " with the phrase "catalytic activity", and to replace the word "mutant" with the word "variant". These amendments serve to more clearly define the invention as claimed in claim 27, and support for these amendments is as described for the amendments to claim 26.

Claim 28 has been amended to recite "activity" after "telomerase", to change the phrase "TP2 mutant" to "telomerase protein 2 variant", and to change the phrase "TP2 biological activity" to "telomerase protein 2 catalytic activity". These amendments serve to clarify the invention as claimed in claim 28, and support for these amendments is as described for claim 26..

Claims 29 and 30 have been amended for clarification to recite that claimed substituted nucleic acid molecules are substituted at nucleotide positions corresponding to the nucleotide sequence of SEQ ID NO:19 (human telomerase 2), and to change the phrase "mutant TP2" to "variant telomerase protein 2".

New claim 33 has been added to capture an additional embodiment of the invention. Support for this claim can be found throughout the specification, as for example, on page 27, lines 25-30 wherein there is a discussion of culturing host cells under appropriate conditions to synthesize telomerase protein 2 polypeptide.

No new matter is added by these amendments.

Rejection Under 35 USC Section 112, First Paragraph

Claims 26-30 have been rejected under 35 USC, Section 112, First Paragraph, as allegedly not enabled by the specification for genes other than SEQ ID NOs:14 and 20, as well as fragments and mutants of these genes. Citing *Ex Parte Maizel* and *In Re Wands*, the Examiner asserts that the specification does not enable any telomerase protein 2 nucleic acid molecule; only the nucleic acid molecule encoding human telomerase protein 2 is enabled.

In response, Applicants assert that the rejected claims are fully supported by the specification. Applicants teach how to obtain non-human telomerase protein 2 nucleic acid molecules in the specification, as for example, on pages 20-21 of the specification. However, solely in the interest of

advancing prosecution of the present invention, Applicants have amended claims 26 and 27 to recite the nucleic acid molecules of SEQ ID NOs:13 or 19, and have amended claims 29 and 30 to recite the nucleic acid molecules of SEQ ID NO:19. Claims 26-28 have been further amended to recite "catalytic activity" in place of "biologically active". Applicants thus respectfully request reconsideration and removal of the rejection under 35 USC, Section 112, First Paragraph.

Rejection Under 35 USC, Section 112, Second Paragraph

Claims 1, 4, 7, 13, 19, and 26-30 have been rejected under 35 USC, Section 112, Second Paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention.

According to the Examiner, "TP2" is vague as it is an abbreviation and does not serve to identify the claimed invention.

In response, Applicants have amended claims 1, 19, 27, 28, 29, and 30 to recite "telomerase protein 2" in place of "TP2".

Claim 1 has been rejected as allegedly indefinite for the use of the "percent sequence identity" language without including an explanation of how the calculation is made.

In response, Applicants respectfully remind the Examiner that the claims are to be read and interpreted in light of the teachings in the specification. Applicants' specification clearly sets forth methods for calculating "percent sequence identity" in great detail. On page 17, lines 1-20, there is a detailed discussion of the computer algorithms that may be used (BLAST and FASTA), together with the scoring matrix (PAM 250) that can be used. However, solely in the interest of advancing the prosecution of claim 1 as well as dependent claims 7, 13, and 19, Applicants have amended claim 1 to recite the calculation parameters.

Claim 1 has further been rejected as indefinite for the use of the term "high stringency conditions" without defining the conditions in the claims. According to the Examiner, the examples of such high stringency conditions set forth on pages 18 and 19 are non-limiting.

In response, the examples of high stringency conditions provided by Applicants show that there are a variety of ways to conduct the hybridization, and any of such methods will work. Thus, a reading of claim 1 in light of this would simply indicate that the skilled artisan could use any of the methods set out by Applicants to conduct the hybridization. However, solely for the purpose of advancing the prosecution of

claim 1, as well as dependent claims 7, 13, and 19, Applicants have incorporated one method of conducting the hybridization into claim 1.

Claim 4 has been rejected as confusing for use of the term "of". The term "of" is an inadvertent typographical error; claim 4 has been amended herein to recite "or" instead.

Claim 26 has been rejected as confusing for use of the phrase "proliferation of a cell". Per the Examiner's suggestion, the claim has been amended herein to recite "proliferation rate of a cell".

Claim 28 has been rejected as confusing for use of the phrase "decreasing telomerase in a cell". In response, this claim has been amended herein to recite "decreasing telomerase activity in a cell".

Claims 29 and 30 have been rejected as indefinite for failure to recite the SEQ ID NO while reciting an amino acid position. In response, Applicants have amended these claims to recite SEQ ID NO:19.

In view of the foregoing, Applicants respectfully request reconsideration and removal of the rejection under 35 USC, Section 112, Second Paragraph.

Rejection Under 35 USC, Section 102(a)

Claims 1, 2, 4, 6-8, 10, 12-14, 16, and 18-19 have been rejected as allegedly anticipated by Nakamura *et al.* According to the Examiner, Nakamura *et a*l. describe the cloning of the putative catalytic subunit of both human and *S. pombe* telomerase. The Examiner asserts that "the gene is identical to the instantly described gene and encodes the same protein". The Examiner points out however that Nakamura *et al.* place the start codon of the encoded protein at amino acid 23. Finally, the Examiner states that she has not been able to review Applicants' priority document, USSN 08/873,039, but that in light of this priority document, Nakamura *et al.* may not in fact constitute prior art.

In response, Applicants assert that Nakamura *et al.* cannot be considered prior art against Applicants' invention at the time it was made and as claimed in claims 1, 2, 4, 6-8, 10, 12-14, 16, and 18-19 for the following reasons. First, the rejected claims of the subject invention are directed to nucleic acid molecules. No nucleic acid molecules are described by Nakamura *et al.*; thus, the Examiner's allegation that "the gene [of Nakamura *et al.*] is identical to the instantly described gene..." is without merit. Given that Nakamura *et al.* does not describe Applicants' claimed nucleic acid molecules, vectors, and host cells, , the reference cannot be considered a proper 102(a) reference.

Next, Nakamura *et al.* describe portions of the amino acid sequence of human telomerase protein 2 (see Figure 2, page 957). Applicants' priority document, USSN 08/873,039, filed 11 June 1997 (more than 2 months prior to the Nakamura *et al.* publication date, sets forth the amino acid sequence of nearly

full length human telomerase protein 2 (see Figures 5 and 6). Thus, Applicants were clearly in possession of the invention directed to human telomerase protein 2 prior to the Nakamura *et al.* publication.

For these reasons, Applicants respectfully submit that this rejection is in error, and request reconsideration and removal of the rejection under 35 USC Section 102(a).

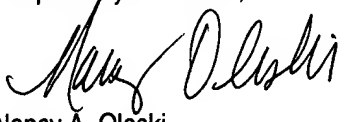
Rejection Under 35 USC, Section 103(a)

Claims 3, 5, 9, 11, 15, 17, 21, 26, and 27 have been rejected under 35 USC, Section 103(a) as allegedly unpatentable over Nakamura *et al.* According to the Examiner, Nakamura *et al.* do not provide the specifically recited fragments or the claimed methods, but do define the shared sequence motifs with other reverse transcriptases, and thus it would have been obvious for the skilled artisan to "subclone regions of the gene". The Examiner further states that Nakamura *et al.* show higher levels of telomerase are expressed in immortal versus mortal cell lines, and therefore it would have been obvious to "place the gene of Nakamura *et al.* into cells, with a reasonable expectation of success in altering endogenous telomerase activity". Finally, the Examiner points out that this reference may not constitute prior art depending on the disclosure of Applicants' priority document 08/873,039.

As discussed above, Nakamura *et al.* cannot be considered prior art against Applicants' claimed invention in light of the contents of Applicants' priority document 08/873,039 filed 11 June 1997. Thus, Applicants respectfully submit that this rejection is in error, and request reconsideration and removal of the rejection.

Applicants believe that the claims as amended herein are in condition for allowance, and a notice to that effect is respectfully solicited.

Respectfully submitted,



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